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PROGNOSTIC FACTORS IN GLIOMA AND A PRELIMINARY EVALUATION OF A NEW SCORING SYSTEM IN SUPRATENTORIAL GLIOMA

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CERTIFICATE

This is to certify that this dissertation entitled **"PROGNOSTIC FACTORS IN GLIOMA AND A PRELIMINARY EVALUATION OF A NEW SCORING SYSTEM IN GLIOMA"** Submitted by Dr.C.J.Biju, appearing for M.Ch (Neurosurgery) Degree Examination in February 2009 is a bonafide record done by him, during the period between June 2004 to February 2009, under my guidance and supervision at the Institute of Neurology , Madras Medical College and Government General Hospital, to the Tamil Nadu Dr.M.G.R Medical University , Chennai .

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CONTENTS

INTRODUCTION

Gliomas account for 40% to 67 % of primary brain tumors (Preston –Martin 1996) and they include astrocytomas, oligodendrogliomas, ependymomas, mixed gliomas [29] .These tumors are neuro-epithelial in origin.

In 1863 Virchow, the founder of cellular pathology coined the term glioma and in 1926 Bailey and Cushing classified these tumors based on histiogenesis , morphological characteristics and biological behaviour and later on was modified by others including Penfield ,Cone and Elvidge .

There has been various other grading systems for gliomas they include Kernohan grading system , St. Anne Mayo and the recent WHO classification[41]. They are based on histological presence of nuclear atypia , mitosis , endothelial proliferation and necrosis .

Of the gliomas , astrocytomas are common and they represent 26.6 % of all newly diagnosed primary brain glial tumors .and oligodendrogliomas 2.1 % (Mahaley 1989) [19].

Gliomas are intrinsic parenchymal lesions of brain which when present in higher grades are associated with mass effect and midline shift and associated with poor prognosis .Gliomas present most commonly with seizures in one half of the patients and in low grade gliomas in the other half patients appear neurologically intact (Schuurman 1997)[35].

The prognosis of these tumors depend on age of the patients , performance scale of the patient , duration of symptoms , pre operative neurological deficit, the extend of resection of tumour , the grade of tumour, adjuvant therapy given and these well known factors have been a

matter of debate and they are analysed in thus study

With the invention of new imaging techniques, microsurgical techniques and adjuvant therapy and other modalities of treatment the prognosis has improved over the years .

There remains a subset of patients in whom the above said therapies when given in an apt manner can improve the outcome .This study was hence undertaken to find the impact of the prognostic factors in the outcome of supratentorial gliomas and to apply a new prognostic scoring in those patient selected .It also aims to find out whether this scoring can be applied in patients with glioma to predict the outcome .

AIM OF STUDY

This study aims at studying the various prognostic factors in supratentorial gliomas and to do a preliminary evaluation of a new prognostic scoring system for supratentorial gliomas

REVIEW OF LITERATURE

There have been many studies on prognostic factors in glioma. Both retrospective and prospective .Many pioneering authors have made studies on age , performance of patients, grading of gliomas , extend of resection and the radiological characteristics.

Even though the gliomas formed 40 to 67 % in a study done by Preston-martin [29] a study done by Dastur , Ramamurthi , Lalitha in 1980 had a lower incidence 35.2 %, 42.5% , 35.8 %, 29.3% in the cities of Mumbai , Delhi, Vellore and Chennai [8].

The incidence of male:female in astrocytomas and oligodendrogliomas is 1.5 : 1 according to Velema (1987) [40] , while Chandra (1983) reported a ratio of 3:1 [5] .

Frontal lobe is the most common location followed by temporal and paraietal lobes is what the studies of Zulch (1986) had concluded [43].

Long duration of symptoms was proven as a favorable factor for survival ina study done by Taekuchi in1977 [38].

Burger & Green (1987) have studied in 71 patients with high grade glioma the role of patient's age , histology features and length of survival of patients [4]

Wood & Shapiro (1988) in 510 patients have studied about the tumor size in computed tomographic scan preoperative and post operatively and had concluded that greater the tumor resection greater the length of survival for the patients [43].

A higher Karnofsky score after surgery was associated with good outcome according to

Winger 1989 [42].

Macdonald (1990) in his retrospective study in 285 patients had concluded that patients with gross total resection lived longer than patients with partial or a biopsy .And they also stated that age , duration of symptoms, pre-operative performance scale , tumor histology, extend of resection and prior low –grade glioma were significant variables influencing survival [17].

Crooks, Waller (1991) have published a detailed account on karnofskys scale in patients of glioma [6].

KARNOFSKY PERFORMANCE STATUS SCALE DEFINITIONS RATING (%) CRITERIA

Able to carry on normal activity and to work; no special care needed.	100	Normal no complaints; no evidence of disease.
	90	Able to carry on normal activity; minor signs or symptoms of disease.
	80	Normal activity with effort; some signs or symptoms of disease.
Unable to work; able to live at home and care for most personal needs; varying amount of assistance needed.	70	Cares for self; unable to carry on normal activity or to do active work.
	60	Requires occasional assistance, but is able to care for most of his personal needs.
	50	Requires considerable assistance and frequent medical care.

Unable to care for self; requires equivalent of institutional or hospital care; disease may be progressing rapidly.	40	Disabled; requires special care and assistance.
	30	Severely disabled; hospital admission is indicated although death not imminent.
	20	Very sick; hospital admission necessary; active supportive treatment necessary.
	10	Moribund; fatal processes progressing rapidly.
	0	Dead

Keeping in mind the general principles of tumor elsewhere in the body , a total excision would be a ideal choice . This is not always possible , because of the location of the tumor in or near a eloquent area , its infiltrating nature and difficulty in ascertaining the precise limits of its extent during surgery (Kornbllith , 1991) [(13)] .

Dedifferentiation or malignant transformation is a well – described phenomenon in low grade gliomas around 13% to 86 % of tumors initially diagnosed as low grade recur at a higher histological grade according to Berger 1994 [(2)] and McCormack 1992 [(21)]

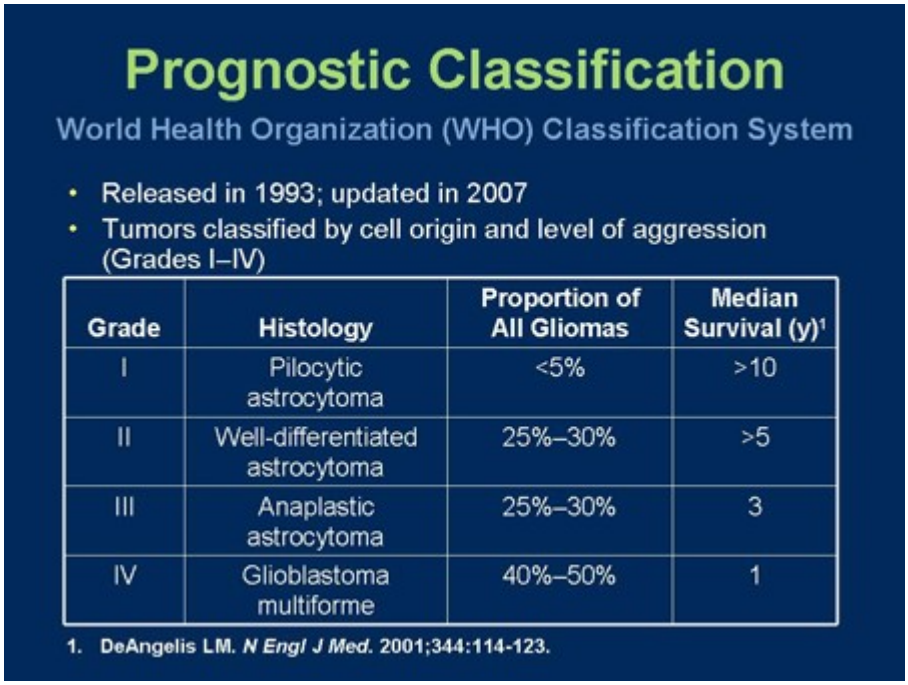
Studies by McCormack 1992 showed that enhancement with contrast in computerized tomogram (CT) had a negative outcome in terms of survival[(21)] .It was also stated by Wu , Lang , Du 1991 that it was not possible to ascertain the grade of malignancy or the histological subtypes using CT [(45)].

Extension into deeper structures and across the midline though not a contraindication for a radical surgery would preclude a surgeon from total excision of the tumor (Tandon 1993)[(37)].

Curran Jr (1993) has prognostically classified gliomas based on age, performance status, Histology , Neurological function , duration of symptoms and extend of resection [(7)].

Macdonald and Mullan in (1994) have studied in 75 patients have quantitatively analysed the extend of resection with pre and post operative scans to determine the effect of extend of resection on survival of patients with astrocytomas [18].

De Angelis (2001) has studied the incidence of symptoms in low grade and high grade gliomas and have found the median survival for the four grades of glioma [9].



Prognostic Classification

World Health Organization (WHO) Classification System

- Released in 1993; updated in 2007
- Tumors classified by cell origin and level of aggression (Grades I–IV)

Grade	Histology	Proportion of All Gliomas	Median Survival (y)[1]
I	Pilocytic astrocytoma	<5%	>10
II	Well-differentiated astrocytoma	25%–30%	>5
III	Anaplastic astrocytoma	25%–30%	3
IV	Glioblastoma multiforme	40%–50%	1

1. DeAngelis LM. *N Engl J Med.* 2001;344:114-123.

The median of low grade gliomas was 35 yrs which was considerably lower than high grade gliomas according to Laws (2001) [16].

Scott (2008) has studied the role of extend of resection in the long-term outcome of low grade hemispheric gliomas [36].

MATERIALS AND METHODS

This study was done in 102 patients of glioma , which was operated in Institute of neurology, Madras Medical College and Government General Hospital, Chennai. This was both prospective and retrospective study with a mean follow up period of 2.5 yrs.

Inclusion criteria :

1. Patients with supratentorial gliomas with preoperative and postoperative contrast computed tomographic scan and with regular followup

Exclusion criteria

1) Patients who did not have a post operative imaging .
2) Patients operated in some other hospital and referred to our hospital

A proforma was made and based on the above criteria 102 patients were selected .It is a prospective and retrospective study .

In retrospective study based on old records patients were enrolled in this study apart from basic investigations computed tomogram plain and contrast was taken and the volume of tumor was calculated based on Di Chiros formula- ***AxBxC/2*** , where **A** is the length, **B** is the breath , **C** is the height of the tumor. The presence of mass effect and edema was noted. The extent of resection was calculated from that formula after taking post operative scan as given in Appendix - III. The follow up ranged from 2 months to 14 years. In the prospective study the patients were followed after admission to the hospital and the details were collected from a period of 2005 to 2008. The details were entered in the Proforma (as given in Appendix – I).

In the post operative period, the performance status of the patient was noted and after histopathological examination the grading of the tumor was recorded and patients were followed after radio therapy and chemotherapy. Based on the above details a master chart was prepared. A new prognostic scoring system for supratentorial gliomas has been evolved in this Institute and a preliminary evaluation of the scoring system has been under taken during this study. The details of the scoring system are given in the table below and master chart was made (seen in Appendix – II).

The effect of various individual prognostic factors and the total score of the new prognostic scale on the outcome on follow up was evaluated using statistical methods. The statistical methods used were SPSS package(Edition 13.0), Pearson Chi-Square, Likelihood Ratio, Fisher's Exact Test and Spearman Correlation.

NEW PROGNOSTIC SCALE FOR SUPRATENTORIAL GLIOMAS

PROGNOSTIC FACTORS	SUB – DIVISIONS	SCORE
AGE	< 45 yrs	3
	45- 64	2
	> 65	1
KARNOFSKYS PERFORMANCE SCALE (KPS)	> 80	3
	50 – 70	2
	< 40	1
DURATION OF SYMPTOMS	1 Yrs	3
	1 month – 1 Yr	2
	< 1 month	1
RADIOLOGICAL PARAMETER	No necrosis, No mass effect	3
	No necrosis, Mass effect	2
	Necrosis and Mass effect	1

GRADING OF TUMOR	Grade 1 &2 Grade 3 Grade 4	3 2 1
EXTENT OF RESECTION	> 95 % Resection < 95 % resection Biopsy	3 2 1

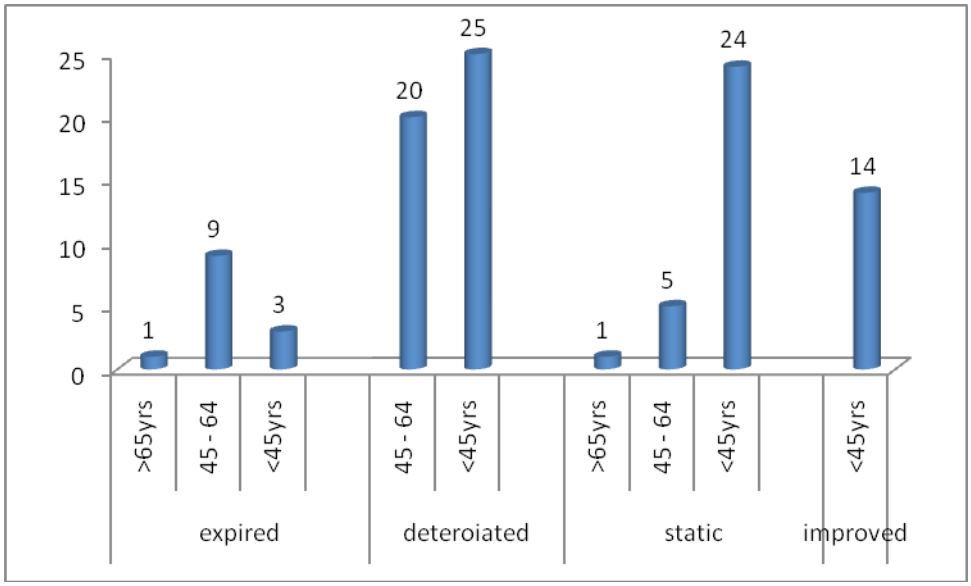
Maximum Score = 18
Minimum Score = 6

RESULTS

AGE Vs OUTCOME

AGE DISTRIBUTION

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	>65yrs	2	1.96	1.960784314	1.960784314
	45 - 64	34	33.33	33.33333333	35.29411765
	<45yrs	66	64.71	64.70588235	100
	Total	102	100.00	100	



Age_r		Frequency
Expired	>65yrs	1
	45 - 64	9
	<45yrs	3
	Total	13
Deteroiated	45 - 64	20
	<45yrs	25
	Total	45
Static	>65yrs	1
	45 - 64	5
	<45yrs	24
	Total	30
Improved	<45yrs	14

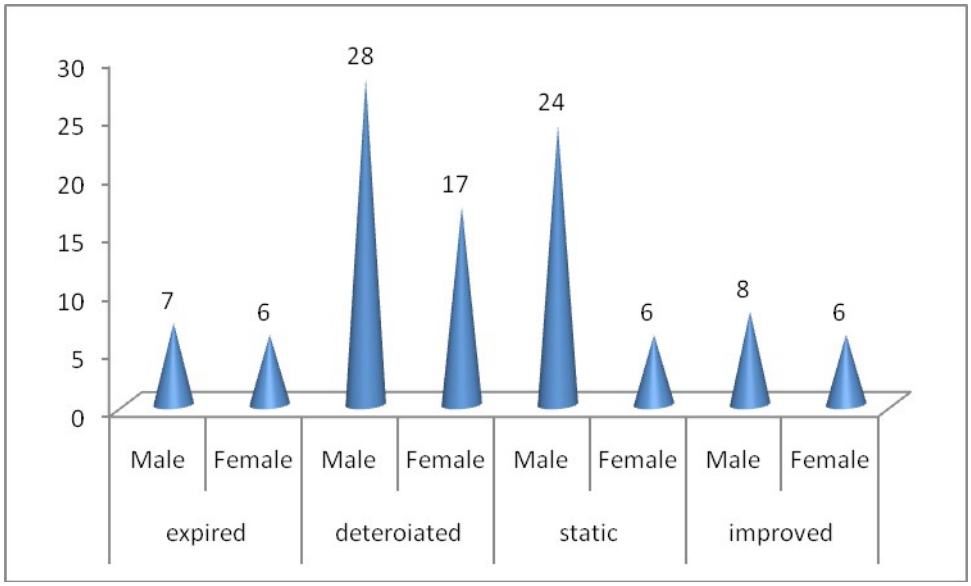
Crosstab-1

		age_r		
	>65yrs 1	45 - 64 2	<45yrs 3	Total
Outcome expired				
deteroiated	0			
static	1	5		
improved	0	0		
Total	2			

In the category of patients who have improved all patients were below the 45 yrs group as evidenced by crosstab test. In the >65 yrs category 50 % of the patients who had glioma expired as in crosstab-1 .

SEX Vs OUTCOME

SEX DISTRIBUTION					
		Frequency	**Percent**	**Valid Percent**	**Cumulative Percent**
Valid	Male	67	65.69	65.68627451	65.68627451
	Female	35	34.31	34.31372549	100
	Total	102	100.00	100	



Sex_r		Frequency
Expired	Male	7
	Female	6
	Total	13
Deteroiated	Male	28
	Female	17
	Total	45
Static	Male	24
	Female	6
	Total	30
Improved	Male	8
	Female	6
	Total	14

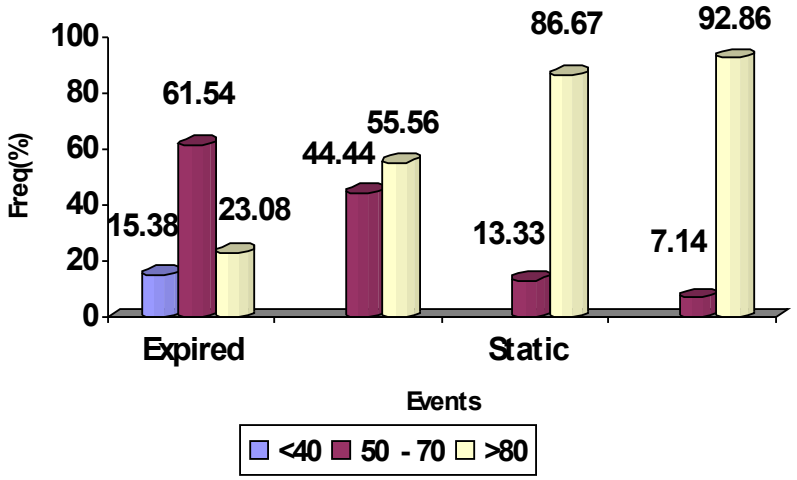
Crosstab 2

		sex_r		
		Male	Female	Total
Outcome	expired	7	6	
	deteroiated			
	static		6	
	improved	8	6	
Total				

Males seem to have higher incidence of gliomas , but there was no significant correlation between males and females in terms of survival and prognosis .

KPS Vs OUTCOME

KPS DISTRIBUTION					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	40 below	2	1.96	1.960784314	1.960784314
	50 - 70	33	32.35	32.35294118	34.31372549
	80 above	67	65.69	65.68627451	100
	Total	102	100.00	100	



KPS_r		Frequency
Expired	40 below	2
	50 - 70	8
	80 above	3
	Total	13
Deteroiated	50 - 70	20
	80 above	25
	Total	45
Static	50 - 70	4
	80 above	26
	Total	30
Improved	50 - 70	1
	80 above	13
	Total	14

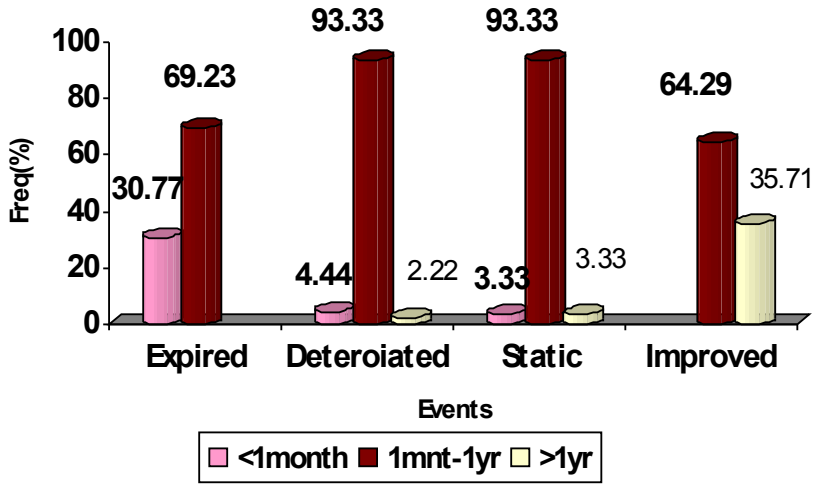
Crosstab 3

		kps_r			
		40 below	50 - 70	80 above	Total
outcome	expired	2	8	3	
	deteroiated	0			
	static	0	4		
	improved	0	1		
Total		2			

There is a significant correlation of outcome and KPS .Patients who had a score below 40 had expired .Most of the patients who had a score above 80 had improved after surgery .

DURATION OF SYMPTOMS Vs. OUTCOME

DISTRIBUTION OF DURATION OF SYMPTOMS					
		Frequency	**Percent**	**Valid Percent**	**Cumulative Percent**
Valid	<1month	7	6.86	6.862745098	6.862745098
	1mnt-1yr	88	86.27	86.2745098	93.1372549
	>1yr	7	6.86	6.862745098	100
	Total	102	100.00	100	



Duration		Frequency
Expired	<1month	4

	1mnt-1yr	9
	Total	13
Deteroiated	<1month	2
	1mnt-1yr	42
	>1yr	1
	Total	45
Static	<1month	1
	1mnt-1yr	28
	>1yr	1
	Total	30
Improved	1mnt-1yr	9
	>1yr	5
	Total	14

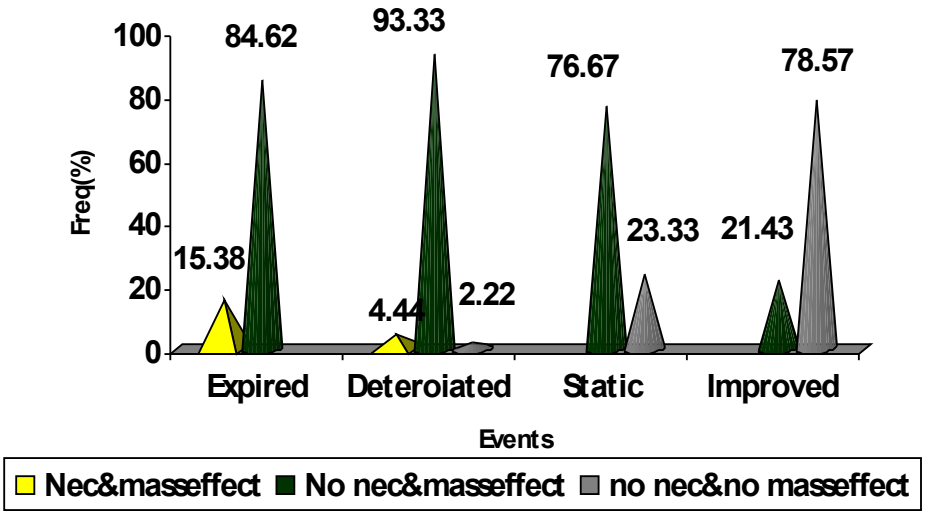
Crosstab 4

		dur		
		<1month	1mnt-1yr	>1yr	Total
expire outcome	deteroiated	2		1	
	static	1		1	
	improved	0	9	5	
Total		7		7	

Patients who were symptomatic for long had improved or remained static after surgery as evidenced by crosstab .But patients who had short duration of symptoms either deteriorated or expired following surgery .

IMAGING FINDINGS Vs. OUTCOME

DISTRIBUTION OF IMAGING FINDINGS					
		Frequency	**Percent**	**Valid Percent**	**Cumulative Percent**
Valid	necrosis & mass effect	4	3.92	3.921568627	3.921568627
	no necrosis, mass effect	79	77.45	77.45098039	81.37254902
	no necrosis, no mass effect	19	18.63	18.62745098	100
	Total	102	100.00	100	



Imaging		Frequency

Expired	necrosis & mass effect	2
	no necrosis, mass effect	11
	Total	13
Deteroiated	necrosis & mass effect	2
	no necrosis, mass effect	42
	no necrosis, no mass effect	1
	Total	45
Static	no necrosis, mass effect	23
	no necrosis, no mass effect	7
	Total	30
Improved	no necrosis, mass effect	3
	no necrosis, no mass effect	11
	Total	14

Crosstab 5

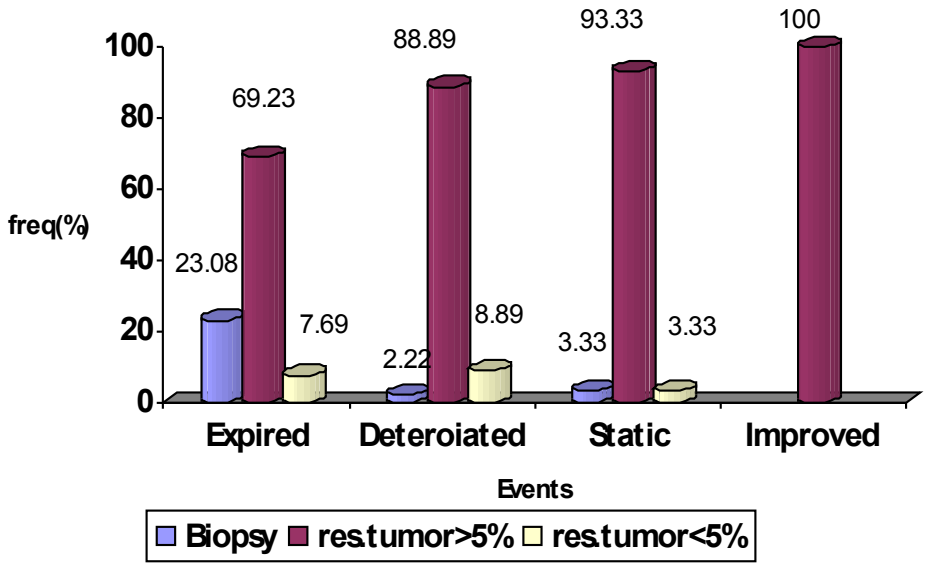
		imaging		
	necrosis & mass effect	no necrosis, mass effect	no necrosis, no mass effect	Total
outcome expired	2		0	
deteroiated	2		1	
static	0		7	
improved	0	3		
Total	4			

Presence of mass effect , edema ,and necrosis is associated with poorer prognosis in terms of survivability and outcome where as patients who did not have the above features had better outcome

EXTENT OF RESECTION Vs. OUTCOME

DISTRIBUTION OF EXTENT OF RESECTION					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	1	5	4.90	4.901960784	4.901960784
	2	91	89.22	89.21568627	94.11764706
	3	6	5.88	5.882352941	100
	Total	102	100.00	100	

- > 95% Resection – 3
- < 95% Resection – 2
- Biopsy – 1



Ext.res		Frequency
Expired	1	3
	2	9
	3	1
	Total	13
Deteroiated	1	1
	2	40
	3	4
	Total	45
Static	1	1
	2	28
	3	1
	Total	30
Improved	2	14

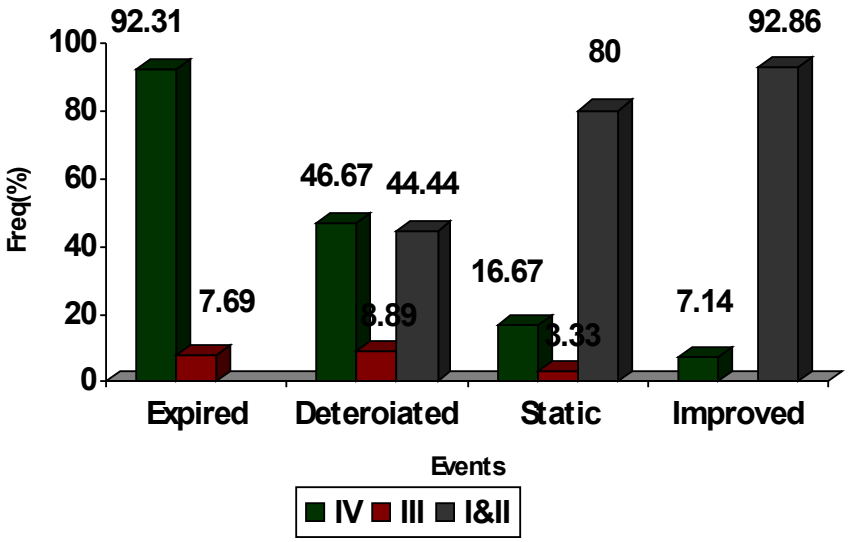
Crosstab 6

		ext.res			Total
		1	2	3	
outcome	Expired	3	9	1	
	deteroiated	1		4	
	static	1		1	
	improved	0		0	
Total		5		6	

More than 95 % resection is associated with increased survivability and in patients in whom only biopsy was done a majority has deteriorated or expired as seen in cross tab test .

GRADING OF TUMOR Vs. OUTCOME

DISTRIBUTION OF GRADING OF TUMOR					
		Frequency	**Percent**	**Valid Percent**	**Cumulative Percent**
Valid	IV	39	38.24	38.23529412	38.23529412
	III	6	5.88	5.882352941	44.11764706
	I&II	57	55.88	55.88235294	100
	Total	102	100.00	100	



Grade_r		Frequency
Expired	IV	12
	III	1
	Total	13
Deteroiated	IV	21
	III	4
	I&II	20
	Total	45
Static	IV	5
	III	1
	I&II	24
	Total	30
Improved	IV	1
	I&II	13
	Total	14

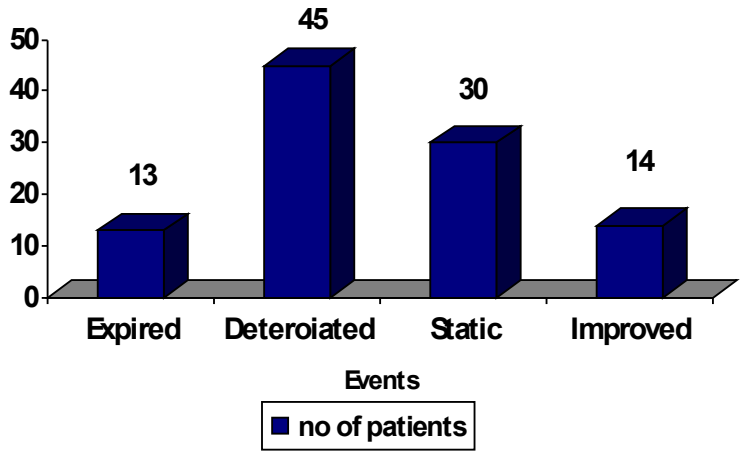
Crosstab 7

		grade_r			
		IV	III	I&II	Total
outcome	expired		1	0	
	deteroiated		4		
	static	5	1		
	improved	1	0		
Total			6		

There is a positive correlation between grading and prognosis. Low grade tumors are associated with good prognosis and higher grade patients are associated with worst prognosis as the above crosstab .

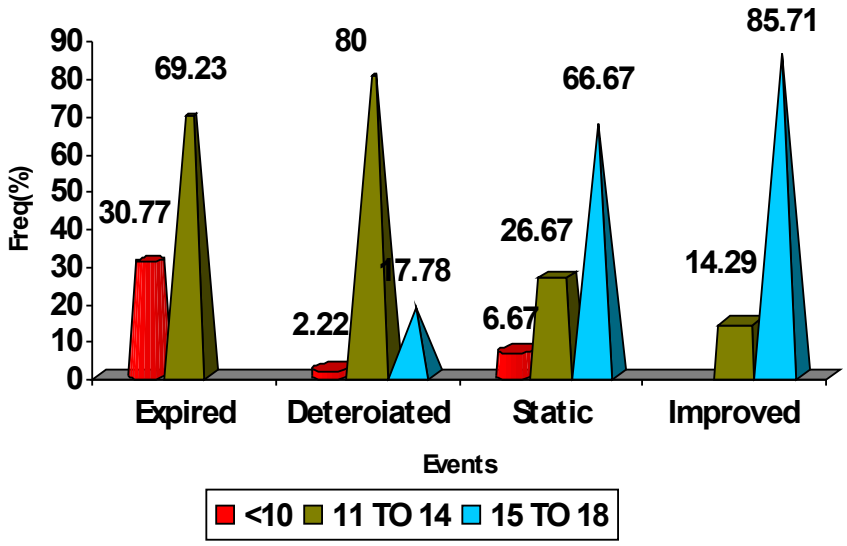
OUTCOME

DISTRIBUTION OF OUTCOME					
		Frequency	**Percent**	**Valid Percent**	**Cumulative Percent**
Valid	expired	13	12.75	12.74509804	12.74509804
	deteroiated	45	44.12	44.11764706	56.8627451
	static	30	29.41	29.41176471	86.2745098
	improved	14	13.73	13.7254902	100
	Total	102	100.00	100	



SCORE Vs. OUTCOME

DISTRIBUTION OF SCORING					
		Frequency	**Percent**	**Valid Percent**	**Cumulative Percent**
Valid	<10	7	6.86	6.862745098	6.862745098
	11-14	55	53.92	53.92156863	60.78431373
	>15	40	39.22	39.21568627	100
	Total	102	100.00	100	



Score_r		Frequency
Expired	<10	4
	11-14	9
	Total	13
Deteroiated	<10	1
	11-14	36
	>15	8
	Total	45

Static	<10	2
	11-14	8
	>15	20
	Total	30
Improved	11-14	2
	>15	12
	Total	14

Score Vs. Outcome : A score < 10 was associated with poor outcome in significant number of patients with supratentorial gliomas. A score > 15 was associated with Good Outcome.

DISTRIBUTION OF NEUROLOGICAL DEFICIT

	Neurological Deficit	Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Attaxic gait	1	0.98	0.980392157	0.980392157
	Dec.vision	1	0.98	0.980392157	1.960784314
	Dysphasia	5	4.90	4.901960784	6.862745098
	Functional.dis	6	5.88	5.882352941	12.74509804
	UMN Faciallag	36	35.29	35.29411765	48.03921569
	Hemiparesis	1	0.98	0.980392157	49.01960784
	Homonymous hemianopia	2	1.96	1.960784314	50.98039216
	Monoparisis	1	0.98	0.980392157	51.96078431

	Nil	22	21.57	21.56862745	73.52941176
	Paraperesis	2	1.96	1.960784314	75.49019608
	Optic atrophy.sec	1	0.98	0.980392157	76.47058824
	Papilloedema	21	20.59	20.58823529	97.05882353
	Slurring speech	1	0.98	0.980392157	98.03921569
	Unconscious	1	0.98	0.980392157	99.01960784
	6^{th} nerve paresis	1	0.98	0.980392157	100
	Total	102	100.00	100	

Hemiparesis and papilloedema was the most common neurological deficit as seen in the above table.

DISTRIBUTION OF SYMPTOMS

	Symptoms	**Frequency**	**Percent**	**Valid Percent**	**Cumulative Percent**
Valid	Alt.sensorium	5	4.90	4.901960784	4.901960784
	Blurring of vision	1	0.98	0.980392157	5.882352941
	Decreased vision	1	0.98	0.980392157	6.862745098
	Headache	56	54.90	54.90196078	61.76470588
	Double Vision	1	0.98	0.980392157	62.74509804
	Headache + vomit	1	0.98	0.980392157	63.7254902
	Hemiparesis	1	0.98	0.980392157	64.70588235
	Focal Seizures	28	27.45	27.45098039	92.15686275
	Generalized Seizures	1	0.98	0.980392157	93.1372549
	Slowness of activity	1	0.98	0.980392157	94.11764706

	Eye Pain	1	0.98	0.980392157	95.09803922
	Vomit	1	0.98	0.980392157	96.07843137
	Weakness	4	3.92	3.921568627	100
	Total	102	100.00	100	

Head ache and Seizures are the most common symptom as seen the above table.

SYMPTOMS Vs. OUTCOME

Outcome	Symptoms	Frequency	Percent
Expired	Alt.sensorium	3	23.08
	Headache	6	46.15
	Hemiparesis	1	7.69
	Seizures	3	23.08
	Total	13	100.00
Deteroiated	Alt.sensorium	1	2.22
	Headache	27	60.00
	Seizures	13	28.89
	Decreased vision	1	2.22
	Slowness of activity	1	2.22
	Vision	1	2.22
	Weakness	1	2.22
	Total	45	100.00
Static	Alt.sensorium	1	3.33
	Headache	14	46.67
	Generalised	10	33.33
	Weakness	3	10.00
	Focal Seizure	1	3.33
	Vomit	1	3.33
	Total	30	100.00

Improved	Headache	9	64.29
	Seizures	2	14.29
	Blurring of vision	1	7.14
	Headache	1	7.14
	Headache + Vomit	1	7.14
	Total	14	100.00

SITE Vs. OUTCOME

Outcome	Site	Frequency	Percent
Expired	C.callosum	2	15.38
	L.frontal	1	7.69
	L.paraietal	2	15.38
	Multifocal	1	7.69
	R.frontal	4	30.77
	R.paraietal	3	23.08
	Total	13	100.00
Deteroiated	C.callosum	3	6.67
	L.frontal	1	2.22
	L.paraietal	12	26.67
	R.frontal	13	28.89
	R.paraietal	2	4.44
	L.temporal	2	4.44
	R.insular	1	2.22
	R.tempora	9	20.00
	R.thalamic	2	4.44
	Total	45	100.00

Static	C.callosum	1	3.33
	L.frontal	1	3.33
	L.paraietal	10	33.33
	R.frontal	9	30.00
	R.paraietal	3	10.00
	L.temporal	2	6.67
	R.tempora	3	10.00
	L.thalamic	1	3.33
	Total	30	100.00
Improved	R.frontal	6	42.86
	R.paraietal	4	28.57
	L.temporal	1	7.14
	R.tempora	1	7.14
	L.thalamic	1	7.14
	Suprasellar	1	7.14
	Total	14	100.00

Right frontal lobe is the most common location of supratentorial gliomas as seen in the above Table.

SPEARMAN CORRELATION

			age_r	sex_r	kps_r	dur	imaging	grade_r	ext.res	event	score_r	totalscore
r s	age_r	Correlation Coefficient	1	-0.01686	**0.270128**	**0.289531**	**0.250369**	**0.401119**	0.143175	**0.456193**	**0.649348**	**0.640569**
		Sig. (2-tailed)	.	0.866425	**0.006037**	**0.003162**	**0.011149**	**2.94E-05**	0.151122	**1.45E-06**	**0.000001**	**0.000001**
		N	102	102	102	102	102	102	102	102	102	102
	sex_r	Correlation Coefficient	-0.01686	1	0.080635	0.05574	-0.17696	0.043176	-0.08471	-0.10032	0.044792	-0.01917
		Sig. (2-tailed)	0.866425	.	0.420445	0.577911	0.075196	0.666555	0.397248	0.315728	0.654856	0.848338
		N	102	102	102	102	102	102	102	102	102	102
	kps_r	Correlation Coefficient	**0.270128**	0.080635	1	**0.345343**	**0.290534**	**0.34368**	-0.01952	**0.476075**	**0.60353**	**0.5902**
		Sig. (2-tailed)	**0.006037**	0.420445	.	**0.000378**	**0.003054**	**0.000405**	0.84561	**0.000001**	**0.000001**	**0.000001**
		N	102	102	102	102	102	102	102	102	102	102
	dur	Correlation Coefficient	**0.289531**	0.05574	**0.345343**	1	**0.242218**	**0.33197**	0.160332	**0.395246**	**0.447005**	**0.524525**
		Sig. (2-tailed)	**0.003162**	0.577911	**0.000378**	.	**0.014176**	**0.000653**	0.107453	**3.93E-05**	**2.48E-06**	**0.000001**
		N	102	102	102	102	102	102	102	102	102	102

imaging	Correlation Coefficient	**0.250369**	-0.17696	**0.290534**	**0.242218**	1	**0.360844**	-0.01165	**0.586792**	**0.496217**	**0.607664**
	Sig. (2-tailed)	**0.011149**	0.075196	**0.003054**	**0.014176**	.	**0.000195**	0.907468	**0.000001**	**0.000001**	**0.000001**
	N	102	102	102	102	102	102	102	102	102	102
grade_r	Correlation Coefficient	**0.401119**	0.043176	**0.34368**	**0.33197**	**0.360844**	1	0.118371	**0.55885**	**0.678988**	**0.841016**
	Sig. (2-tailed)	**2.94E-05**	0.666555	**0.000405**	**0.000653**	**0.000195**	.	0.236047	**0.000001**	**0.000001**	**0.000001**
	N	102	102	102	102	102	102	102	102	102	102
ext.res	Correlation Coefficient	0.143175	-0.08471	-0.01952	0.160332	-0.01165	0.118371	1	0.044649	0.195495	**0.219566**
	Sig. (2-tailed)	0.151122	0.397248	0.84561	0.107453	0.907468	0.236047	.	0.65589	0.04894	**0.026602**
	N	102	102	102	102	102	102	102	102	102	102
event	Correlation Coefficient	**0.456193**	-0.10032	**0.476075**	**0.395246**	**0.586792**	**0.55885**	0.044649	1	**0.60803**	**0.734251**
	Sig. (2-tailed)	**1.45E-06**	0.315728	**0.000001**	**3.93E-05**	**0.000001**	**0.000001**	0.65589	.	**0.000001**	**0.000001**
	N	102	102	102	102	102	102	102	102	102	102
score_r	Correlation Coefficient	**0.649348**	0.044792	**0.60353**	**0.447005**	**0.496217**	**0.678988**	0.195495	**0.60803**	1	**0.895587**
	Sig. (2-tailed)	**0.000001**	0.654856	**0.000001**	**2.48E-06**	**0.000001**	**0.000001**	0.04894	**0.000001**	.	**0.000001**
	N	102	102	102	102	102	102	102	102	102	102
totalscore	Correlation Coefficient	**0.640569**	-0.01917	**0.5902**	**0.524525**	**0.607664**	**0.841016**	**0.219566**	**0.734251**	**0.895587**	1
	Sig. (2-tailed)	**0.000001**	0.848338	**0.000001**	**0.000001**	**0.000001**	**0.000001**	**0.026602**	**0.000001**	**0.000001**	.
	N	102	102	102	102	102	102	102	102	102	102

Correlation is significant at the 0.01 level (2-tailed).

Correlation is significant at the 0.05 level (2-tailed).

Coefficients(a)

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	6.59433E-15	3.76E-08		1.75E-07	1
	age_r	1	8.55E-09	0.257316	1.17E+08	0
	kps_r	1	8.64E-09	0.256089	1.16E+08	0
	dur	1	1.2E-08	0.182461	83279701	0
	imaging	1	9.63E-09	0.22237	1.04E+08	0
	ext.res	1	1.23E-08	0.161663	81001131	0
	grade_r	1	4.91	0.469825	2.03E+0	0

			E-09		8	
a	Dependent Variable: totalscore					

In the Spearman correlation the preoperative Karnofskys performance status of the patients , Grading of the tumor , presence of necrosis in imaging all correlated significantly with the outcome.Other factors like age , duration of symptoms and extent of resection had a less significant correlation . The prognostic scoring applied in patients to predict the outcome had a significant correlation .

DISCUSSION

There have been various studies analyzing the impact of various prognostic factors on the outcome in gliomas. Age, duration of symptoms, preoperative KPS, CT appearance, extent of resection and histological grade have been found to be the most important among the various factors affecting the outcome in gliomas (Burger and Green 1987) (Ammirati 1987) (Burger 1994) (Keles 2001)(Mariani 2004) (Nakamura2000)(Pignatti 2002) (Scerrati 1996) (2,1,11,13,24,28,33.)

Age as an important factor in determining the outcome has been emphasised in various studies. Burger and Green (1987) found negative relationship between advancing age and duration of postoperative survival in glioblastomas[2].Laws et al (1984) found age of the patient was by far the most important variable in predicting length of survival[17]. Scerrati et al (1996) found significant positive association with survival at univariate analysis was found for the age group < 20 years, for total and subtotal surgical resections in low grade gliomas[33]. In the present study, age less than 45 years correlated with better outcome than the other age groups. But age was not a major prognostic factor.

Duration of symptoms as a major prognostic factor has been emphasized by Takeuchi et al (1977)[38]. In the present study also duration of symptoms more than one year favoured good outcome.

Preoperative KPS as a major prognostic factor has been documented by Scerrati et al (1996)[33], Nakamura et al (2000) and Winger et al (1989)[24,42]. In the present study,

preoperative KPS had a very significant impact on the outcome. KPS more than 80 favoured a good outcome.

CT Scan findings were found to influence the outcome by many authors. Wood et al (1988) have found that tumor size on the CT Scan was of prognostic importance independent of the other known prognostic variables[43]. Schuurman and Troost (1997) found that presence or absence of contrast enhancement on CT was an important prognostic factor[35]. McCormack et al (1977) also contrast enhancement on CT had a negative outcome in terms of survival[21]. Berger et al (1994) highlighted the importance of tumour necrosis as a prognostic factor[2]. In the present study presence of tumour necrosis and mass effect in the pre-operative CT affected the outcome adversely.

Extent of tumour resection has been projected as the major prognostic factor by many authors. Gross total resection of supratentorial glioblastomas and anaplastic astrocytomas is feasible and is directly associated with longer and better survival when compared to subtotal resection (Ammirati et al, 1987)[1]. Scerrati et al (1996) have found that the most relevant factor affecting survival at the multivariate analysis was the extent of surgical resection[33]. This has also been emphasized by Macdonald et al (1990), Wood and Shapiro (1988), Winger et al (1989), Mariani et al (2004), Nakamura et al (2000), Keles et al (2004), Tandon et al (1986) [18,43,42,20,12,39]. In the present study, gross total resection with residual tumour less than 5% had very favourable outcome. Those who had biopsy alone fared poorly.

Histological grade has a very important significance. This has bee highlighted in the studies of Winger et al (1989), Scerrati et al (1996), Pignatti et al (2002), Nakamura et al (2000), Mariani et al (2004) [42,33,28,20]. In the present study also the histological grade of the tumour was a major prognostic factor. Patients with low grade (Grade I & II) fared well.

Majority of patient with grade III deteriorated functionally and majority with Grade IV tumours expired.

Various attempts at prognosticating the outcome in gliomas have been made. Pignatti et al (2002) used age > or = 40 years, astrocytoma histology subtype, largest diameter of the tumor > or = 6 cm, tumor crossing the midline, and presence of neurologic deficit before surgery as unfavorable prognostic factors for survival[28]. The total number of unfavorable factors present were used to determine the prognostic score. Schuurman and Troost (1997) used age, duration of symptoms, pre-operative neurological examination and CT-contrast enhancement to evolve a prognostic score. Numerical scoring was performed by giving either 1 or 0 for: age > or < 40 years, symptom duration < or > 1 year, presence or absence of focal deficit, and presence or absence of CT-contrast enhancement, combining these factors in a score ranging from 0-4[35]. Curran et al (1993)[7] have devised a prognostic classification which is given the following table:

Prognostic Classification

RTOG Recursive Partitioning Classification System

- Patients with high-grade gliomas identified in the Radiation Therapy Oncology Group (RTOG) database
- Stratification into groups (Class 1–6) based on
  - Age
  - Performance status
  - Histology
  - Neurological function
  - Duration of symptoms
  - Extent of resection
- Prognostic variables may be used to compare trial data

Class	Median Survival (mo)	2-Year Survival (%)
1	59	76
2	37	68
3*	18	35
4*	11	15
5*	9	6
6*	4.5	4

*GBM.

Curran WJ Jr, et al. *J Natl Cancer Inst.* 1993;85:704-710; with permission.

The new prognostic scoring system evolved in this Institute, incorporating all the important prognostic factors like age, duration of symptoms, preoperative KPS, CT findings, histological grade and extent of resection is a very simple, easy to apply and has a good predictive value. Majority of patients having a score of 15 and more had good quality of survival; majority of patients with score 10 and less expired; majority of those with score 11 to 14, deteriorated in quality of life.

LIMITATIONS OF THE STUDY

1) The patients have been treated by different neurosurgical units with different protocols.
2) In this study only KPS on follow up has been used to determine the outcome . The length of survival has not been studied .
3) Follow up period for prospective patients were short.
4) Only quality of survival has been studied and duration of the survival has not been studied.

CONCLUSIONS

A study of various prognostic factors on the outcome of 102 supratentorial gliomas has been done and the following conclusions have been drawn from this study

1) Preoperative Karnofsky performance scale (KPS) , imaging and histological grading of the tumors were the most important prognostic factors affecting the outcome in supratentorial gliomas.

2) Age , duration of symptoms , extent of resection were less significant in determining the outcome.

3) The new prognostic scoring system for supratentorial gliomas is found to be very simple , devoid of any complex formulae or tables and easy to apply , it also correlates well with the outcome.

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APPENDIX – I

PROFORMA

Name Age Sex I.P. No M.I.N No Unit

Contact Address / No

D.O.A.

D.O.S

D.O.D

CLINICAL DATA PRE OPERATIVE KPS :

NEUROLOGICAL DEFICIT :
SYMPTOMS & DURATION :

RADIOLOGICAL PARAMETER

VOLUME OF TUMOR
EDEMA
MASS EFFECT
MORPHOLOGY
BASAL CISTERNS

HISTOLOGY :

GRADING

SITE OF TUMOR

SURGERY :

EXTENT OF RESECTION AS DEDUCTED BY POST OPERATIVE CT

POST OPERATIVE FOLLOW UP

ADJUNCT THERAPY

FOLLOW UP PERIOD: KPS :

OUTCOME

IMPROVED

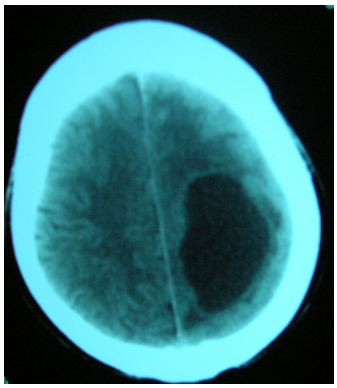
STATIC

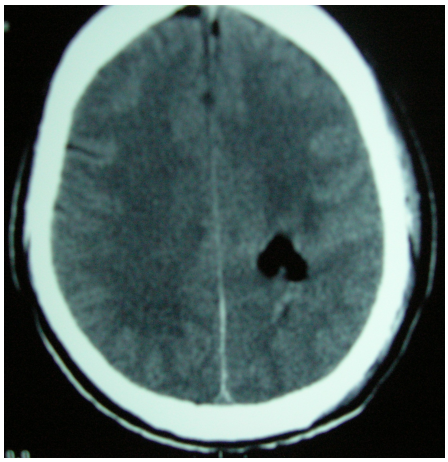
DETORIATED

EXPIRED

APPENDIX – III
EXTENT OF RESECTION

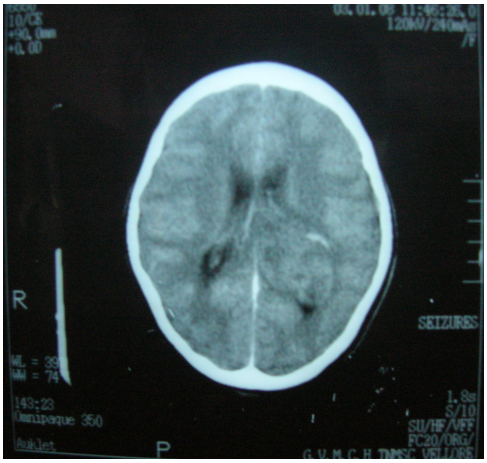
(A) > 95% RESECTION

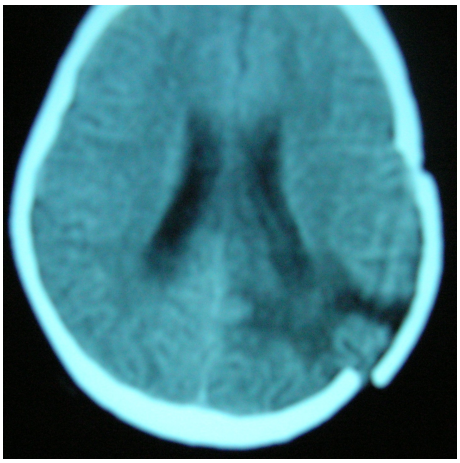




PRE OPERATIVE **POST OPERATIVE**

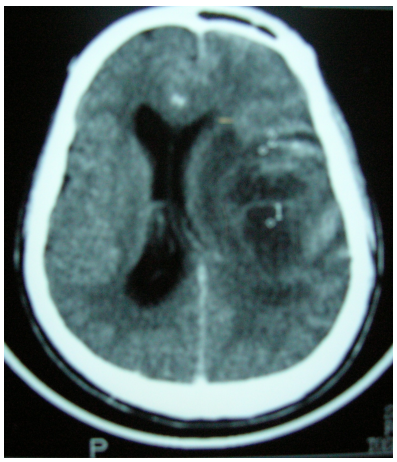
(B) < 95% RESECTION



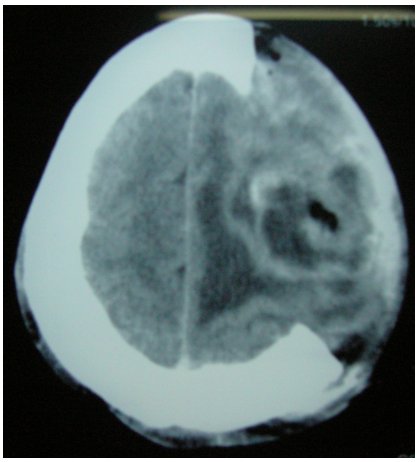


(C) BIOPSY **POST OPERATIVE**

PRE OPERATIVE



POST OPERATIVE



A : > 95% Resection

B : < 95% Resection

C : Biopsy